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S1 ATP Synthase

1L1

Subunit rotation and twisting in F_oF_1-ATP synthase by single-molecule three-color Förster resonance energy transfer

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Catalytic activities of enzymes are associated with elastic conformational changes of the protein backbone. These conformational changes of single proteins can be monitored in real time by Förster resonance energy transfer, FRET. Two different fluorophores have to be attached to those protein domains, which move during function. Distance fluctuations between the fluorophores are measured by relative fluorescence intensity changes or fluorescence lifetime changes.

F_oF_1-ATP synthase is a rotary molecular machine which catalyzes the formation of adenosine triphosphate (ATP) known as the 'energy currency' of the living cell. The *Escherichia coli* enzyme consists of a membrane-bound F_o motor where proton translocation through F_o drives a 10-stepped rotary motion[1]. An internal central stalk transduces the energy of this rotation to the F_1 motor, where ATP is synthesized in an 120° rotary stepping cycle[2, 3]. The exact mechanism of energy storage to bridge the symmetry mismatch of the two motors with different step sizes is not fully understood. The rotary mechanics of proton-driven F_oF_1-ATP synthase will be discussed and a new single-molecule FRET approach to observe both rotations simultaneously in a triple-labeled single F_oF_1-ATP synthase at work will be presented[4].

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1L2

Specificity, mechanism and membrane organization of ATP synthases

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High-end molecular simulation methods in synergy with structural and functional studies are providing novel and important insights into the mechanism and organization of ATP synthases. I will present an overview of our progress in this area, at first focusing on the membrane motor. Building upon our previous theoretical studies of the structural basis for the distinct ion specificity of enzymes from different species [1], we have recently contributed to uncover a subclass of ATP synthases concurrently driven by proton and Na^+ gradients under physiological conditions [2], a new paradigm in membrane bioenergetics. Computer simulations have also shed light into the gating mechanism of the ion binding sites in the c-ring, a key element in the membrane motor, and have suggested that hydration of these sites plays a central role [3]. These findings have been confirmed experimentally by recent structural studies of a mitochondrial c-ring, at atomic resolution [4]. Molecular models of a subcomplex consisting of the c-ring and subunit-a, derived from state-of-the-art structure prediction algorithms and guided by extensive cross-linking and accessibility data, help to rationalize how ions and water reach the binding sites in the c-ring [5]. To conclude, I will describe new investigations into the organization of ATP synthases in mitochondrial membranes, and discuss how these fascinating enzymes might contribute to define the morphology of mitochondria [6].

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